Remarks

Amendments to the Claims

Claim 2 is amended to clarify which cells of the tissue express the suicide gene product. The amendment does not add new matter.

Information Disclosure Statement

The Office Action states that several references cited in the IDS filed on March 4, 2005 are not present in the file for this application. Copies of the missing documents (Bernstein; Wang) are provided with this paper.

Abstract

The specification is objected to because the abstract does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). An abstract on a separate sheet accompanies this paper. The abstract is identical to the abstract filed with the application and does not add new matter.

Rejection of Claims 1, 2, 4, 5, 7, and 8 Under 35 U.S.C. § 102(e)

Claims 1, 2, 4, 5, 7, and 8 stand rejected under 35 U.S.C. § 102(e) as anticipated by Wu, U.S. Patent 6,995,299. Applicants respectfully traverse the rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The identical invention must be

shown in as complete detail as is contained in the claimed invention. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

Claim 1 is directed to a method of engrafting foreign replacement cells within a fetal non-human mammal. The method comprises two steps: (a) selectively destroying native cells in a tissue of a fetal non-human mammal host, wherein the number of maternal cells of the same tissue is not substantially reduced; and (b) implanting foreign replacement cells in the tissue of the fetal non-human mammal host, whereby the foreign replacement cells replace destroyed cells of the tissue. Wu does not teach a method of engrafting foreign replacement cells within a fetal non-human mammal comprising the steps recited in claim 1.

Wu does not describe engrafting foreign replacement cells within a fetus. Rather, Wu describes inducing tolerance in a fetus and then "introducing human hepatocytes into the tolerized animal, preferably postnatally and preferably by intra-splenic injection." See column 5, lines 6-8. Example 10.1.4 describes Wu's cellular transplantation method:

> Within 24 hours of birth, newborn rats were placed on ice for 2-5 minutes. Then under sterile conditions, left paracostal incisions were made and primary human hepatocytes, Huh7, or HepG2 cells, $1x10^7$ cells/ml in 200 µl PBS were injected into the spleen by sterile Hamilton syringe.

Wu, column 42, lines 27-32. Wu describes introduction of hepatocytes postnatally and does not teach implanting foreign replacement cells in the tissue of the fetal non-human mammal host, as recited by claim 1. Thus, Wu does not anticipate claim 1 because Wu does not teach each and every element of the claim.

Please withdraw the rejection.

Rejection of Claims Under 35 U.S.C. § 103(a)

Claims 1 and 3 stand rejected under 35 U.S.C. § 103(a) as obvious over Wu in view of Loeb (U.S. Patent 6,451,571). Claims 1 and 9-12 also stand rejected under 35 U.S.C. § 103(a) as obvious over Wu in view of Sorscher (U.S. Patent 6,017,896). Applicants respectfully traverse both rejections.

The U.S. Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of obviousness. The *prima facie* case requires that the prior art reference (or references when combined) must teach or suggest all the claim limitations. Manual of Patent Examining Procedure, 8th ed., § 2142. The Patent Office has not made a *prima facie* case of obviousness because the cited references, even if combined, do not teach or suggest all the claim limitations.

As discussed above, Wu does not teach the step of implanting foreign replacement cells in the tissue of a fetal non-human mammal host. In fact, Wu teaches away from introducing foreign replacement cells in a fetus, because Wu teaches that the foreign replacement cells preferably are introduced postnatally (*see, e.g.*, col. 5, lines 6-8; and Example 10.1.4).

The Office Action cites Loeb "for a mutated thymidine kinase," and for providing "the motivation to substitute mutated thymidine kinase for the wild type form . . . ." Office Action at page 5, lines 17-19. Nowhere does Loeb teach or suggest implanting foreign replacement cells in the tissue of the fetal non-human mammal host. Thus, Loeb does not cure the deficiencies of Wu. The Patent Office has failed to make a *prima facie* case of obviousness because the Wu and Loeb references, even if combined, do not teach or suggest all the claim limitations.

The Office Action cites Sorscher as describing "a method of killing replicating or non-replicating mammalian cells transduced with a nucleic acid encoding non-human purine cleavage enzyme and contacting the transduced cells with a substrate for the enzyme." Office Action at page 6, lines 13-16. The Office Action also cites Sorscher as teaching liposomes and immunoliposomes. See Office Action at page 6, lines 18-24. Nowhere does Sorscher teach or suggest implanting foreign replacement cells in the tissue of the fetal non-human mammal host. Thus, Sorscher does not cure the deficiencies of Wu. The Patent Office has failed to make a *prima facie* case of obviousness because the Wu and Sorscher references, even if combined, do not teach or suggest all the claim limitations.

Please withdraw the rejections.

Respectfully submitted,

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